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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,969	05/08/2001	Randolph J. Noelle	037003-0280613	1327

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,969	NOELLE, RANDOLPH J.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 4/1/05

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application. 1, 5-10, 12-14, 17, 19

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected. 1, 5-10, 12-14, 17, 19

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 4/1/05, has been entered.
Claims 1, 8 and 12-14 have been amended.

Claims 1, 5-10, 12-14, 17 and 19 are pending and being acted upon presently.

Claims 4, 15, 16, 18, 20 and 21 have been canceled.
Claims 2, 3 and 11 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments in the amendment, filed 4/1/05.
The rejections of record can be found in the previous Office Action.

3. Applicant's amended claims, filed 4/1/05, have obviated the previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "a cell-mediated immune reaction".

4. Claims 1, 5-10, 17, and 19 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed:
"wherein the tissue destruction results from a T cell-mediated immune reaction to one or more autoantigens"
AND, in a New Grounds of Rejection,
"wherein the anti-gp39 antibody or fragment binds to an epitope which is specifically bound by a monoclonal antibody produced by the 24-31 hybridoma".

Applicant's amendment, filed 4/1/05, directs support to page 9, Example 1, where three (3) autoantigens can induce the T cell mediated autoimmune disease EAE in mice.
In addition, applicant asserts that the term "autoantigens" as well as the specific embodiments of auto antigens are plural, thereby supporting the phrase "one or more".

It appears that applicant acknowledges that these particular "phrase" does not have written description in the specification as filed; therefore the claims represent a departure from the specification and claims as originally filed.
Applicant's reliance on generic disclosure and possibly a single or limited species (e.g. Example 1 on pages 9-11 of the specification, drawn to one set of mouse autoantigens in one experimental mouse model) do/does not provide sufficient direction and guidance to the features of "one or more", as currently claimed.
Further, it appears that Example 9 describes administration the mouse autoantigens in the alternative (see page 9, second sentence of the second paragraph of Example 1) and not in a manner consistent with " one or more", as currently claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Applicant's amendment, filed 4/1/05, does not provide sufficient direction for the written description: "wherein the anti-gp39 antibody or fragment binds to an epitope which is specifically bound by a monoclonal antibody produced by the 24-31 hybridoma".

Here again, applicant's presumed reliance on generic disclosure of anti-gp39 antibodies (see pages 4-6 of the specification) and a single species of anti-gp39 antibodies produced by the 24-31 hybridoma (see page 6, paragraph 2 of the instant specification) do/does not provide sufficient direction and guidance to the features of establishing a new subgenus "an 24-31 antibody epitopic specificity", as currently claimed

The specification as filed does not provide a sufficient written description of specific "limitations" within this newly submitted phrase. The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action

Alternatively, applicant is invited to provide sufficient written support for the "imitations" indicated above. See MPEP 714.02 and 2163.06

4. Upon reconsideration of applicant acknowledgement in conjunction with Janssen v. Rexall Sundown, 68 USPQ2d 1154 (Fed. Cir. 2003) that the claims are intended to read on preventing further tissue destruction during treatment of type I diabetes following diagnosis, the previous rejection under 35 U.S.C.§ 112, first paragraph, enablement with respect to "preventing" has been withdrawn.

5. Applicant's amended claims, filed 4/1/05 have obviated the previous rejections under 35 U.S.C.§ 112, second paragraph, with respect to the recitation of
"or an antibody having the gp39 binding characteristics thereof" and
in the recitation of "24-31".

6. Claims 12-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-14 are indefinite in the recitation of "T cell mediated autoimmune responses associated with type I diabetes" in that the nature or parameters of said "autoimmune responses are ill-defined and ambiguous.

Applicant argues in conjunction with an attached Abstract by Rabinovich that as of the earliest filing date, T cell mediated autoimmune responses associated with type I diabetes were well known,
However, the examiner could not locate the Rabinovich Abstract.

Applicant is invited to provide evidence to support their assertions, including the submission of the Rabinovich Abstract.
The examiner apologizes for any inconvenience to applicant in this matter.

Again applicant is invited to amend the claims to recite specific endpoints that can be measured.

Applicant should specifically point out the support for any amendments made to the disclosure.
See MPEP 714.02 and 2163.06

7. For examination purposes, the claims can be read on preventing the elaboration of T cell mediated tissue destruction / autoimmune responses associated with type I diabetes as part of a therapeutic regimen during the treatment of type I diabetes rather than being limited to preventing type I diabetes per se.

8. Upon reconsideration of applicant's amended claims and arguments, filed 8/26/04, the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Noelle et al. (U.S. Patent No. 5,683,693) has been withdrawn.

9. Given applicant's arguments and the Noelle affidavit concluding that the 5c8 and 24-31 antibodies bind different epitopes on human CD154 (gp39, CD40 ligand),
the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Lederman et al. (U.S. Patent No. 6,592,868), has been withdrawn.

10. Claims 1, 5-10, 12-14, 17 and 19 are rejected under 35 U.S.C.§ 103(a) as being unpatentable Lederman et al. (U.S. Patent No. 6,592,868) in view of Noelle et al. (U.S. Patent No. 5,747,037) for the reasons of record.

Applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Although the 5c8 antibody and the instant 24-31 antibody epitope specificities nor describe "T cell mediated autoimmune responses" per se,
the prior art , including both Lederman et al. and Noelle et al. clearly provided for inhibiting cell-mediated inflammatory conditions, autoimmunity or diabetes at the time the invention was made with 5C8-specific / CD40L-specific antibodies.
The prior art teaching of Lederman et al. is not limited to treating B cell immune responses only, given its teaching of inhibiting transplant rejection and autoimmune diseases such as diabetes.

Although applicant argues that there is no suggestion in the '037 in merely admininstering the gp39 antagonist without antigen,

Lederman et al. does teach treating diabetes with 5c8- (gp39-, CD40 ligand-) specific antibodies in the absence of antigen presenting cells.

In addition, autoimmunity by its very nature encompasses the presence of autoantigen.

'037 provides for a more efficient method for inducing long term specific nonresponsiveness to autoantigens by providing antigen presenting cells in methods to treat an autoimmune condition such as diabetes, already taught to be treated with CD40 ligand-specific antibodies in the absence of antigen presenting cells by Lederman et al.

Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

Given the assertionsof unexpected results, the prior art already provides clear direction in providing for the particular 24-31 CD40 ligand-specific antibody in the treatment of diabetes at the time the invention was made.

In this case the teachings of both the primary and second references indicate success in treating diabetic patients with anti-CD40 ligand antibodies in the face of having to solve the same or nearly the same problem would have led one of ordinary skill in the art at the time the invention was made to combine the references to treat the same or nearly the same diabetic patient populations with antagonistic therapeutic anti-CD40 ligand antibodies to dampen the well known inflammatory problems associated with diabetic patients in the art.

The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

In response to applicant's arguments against the references individually, one cannot show non - obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's assertions of unexpected results do not overcome clear evidence of obviousness of treating patients with diabetes with anti-CD40 ligand antibodies, including the 24-31 antibody at the time the invention was made

As pointed out previously, although Lederman is silent about the prevention of a T cell mediated autoimmune response associated with type I diabetes, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

"{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. "In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

Given the antagonistic properties of the particular 24-31 and 89-76 CD40L-specific antibodies taught by Noelle et al. (>037), the ordinary artisan would have been motivated to substitute these CD40L antagonists into the methods of treating autoimmune diseases such as diabetes, as taught by Lederman, given their inhibitory properties were consistent with the antagonistic CD40L-specific antibodies taught by the prior art. Noelle et al. (>037) and Lederman et al. all teach the advantages of anti-CD40L antibodies to inhibit immune responses by targeting the CD40L on T helper cells in therapeutic modalities of immunosuppression at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

11. No claim allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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June 6, 2005